Ex. 11

EXHIBIT 11

NDA LOG

SubType: NDA

CI#: 376 | Sub Date: 12/27/90

Generic: | Appr Date:

Product Name: Estrostep Tablets

Barcode	Ser/ Ref#	Date / To: / From:	RE/ Report Title/ Report No. / Contents/Report No./
B04551	1	Thu, Dec 27, 1990	Initial NDA (Volumes 1.1 - 1.63)
			Item 1: Table of Contents. Item 2: Comprehensive Summary. Item 3: Chemistry, Manufacturing and Controls. Item 4: Samples, Methods and Labeling. Item 5: Item 6: Human Pharmacokinetics and Bioavailability. Item 7: Item 8: Clinical Data. Iem 9: Item 10: Statistical Data. Item 11: Case Report Tabulations. Item 12: Case Report Forms. Item 13: Patient Information. (1) Research report submitted. Refer to Research Report list for RR#, date, author and title.
B04602		Thu, Jan 03, 1991	Letter From FDA Acknowledging Receipt of NDA (NDA 20-130)
			Re: Acknowledgement of receipt of NDA n 28-Dec-90; Number 20-130 assigned.
		J. Short	
B04602	2	Fri, Feb 08, 1991	Letter Re: Amendment to Estrostep NDA Items 3 & 4
		S. Sobel	CI-376 Re: Amendment to Items 3 and 4 of the Estrostep NDA, information enclosed.
B04602		Thu, Mar 14, 1991	Letter Re: Pending New Drug Application for Estrostep-21
			CI-376 Re: Enclosed copy of the minutes for the fertility and maternal health drugs advisory committee; the committee discussed family health international's proposal to standarize and simplify the patient directions for use.
		S. Sobel	
B04602	3	Thu, Mar 28, 1991	Letter Re: Amendment
		S. Sobel	CI-376 Re: Attached information requested by Dr. Rarick on 20-Mar-91.

SubType: NDA

CI#: 376 Sub Date: 12/27/90

Generic: Appr Date:

Product Name: Estrostep Tablets

Barcode	Ser/ Ref#	Date / To: / From:	RE/ Contents/Report No./ Report Title/ Report No.
B04603		Fri, Apr 19, 1991 G. Turner	Letter Re: Request of 17-Apr-91 Re: Per your request of Apr 17, 1991, attached is a copy of clinical Protocol 376-364 and three volumes of case report forms (CRF's) from Estrostep (NDA 20-130). Volume I contains cover letter and PR. 376-364. Volume II contains the CRF's from Site 3, every tenth patient. Walter Schoen, M.D. Volume III contains the CRF's from Site 5, every fifteenth patient. Charles Veale, M.D. Volume IV contains the CRF's from Site 6, every fifteenth patient. James Geil, M.D. Each volume is tabbed according to patient number. If you have any questions, please feel free to call ------
B04602	4	Fri, Apr 19, 1991 S. Sobel	Letter Re: Case Report Forms Re: For your information and files attached is a copy of the cover letter sent to Dr. G. Turner of the FDA's divisional scientific investigations, clinical investigations branch. We have supplied Dr. Turner with case report forms for Site 3, 5 and 6 of the Estrostep clinical study 376-364. If you have any questions, please contact me.
B04605	5	Mon, Apr 22, 1991 S. Sobel	Letter Re: Amendment to Estrostep NDA Item 3 Re: Reference is made to our new drug application (NDA #20-130) for Estrostep (norethindrone acetate and ethinyl estradiol, USP) tablets for oral contraception submitted on December 27, 1990. Dr. Martin Benett of your division, in a phone conversation with Dr. Sean Brennan (Parke-Davis) on April 11, 1991, requested the addresses of the maufacturing facilities for the drug substances, norethindrone acetate and ethinyl estradiol. We are amending the following to Item 3 of the NDA. As noted in the attached letters from the suppliers, the addresses are: See attached; Continued - see central file copy.
B04605	6	Fri, Apr 26, 1991 S. Sobel M. Taylor	Letter Re: 4-Month Safety Update (Volumes 3.1 - 3.2) Re: Attached is the 4-month safety update for the Estrostep NDA 20-130. The original integrated summary of safety summarized data from one clinical pharmacology study (376-372) and on clinical study (376-364), through a cut-off date of March 28, 1990. The safety update summarizes the safety data from 2 clinical pharmacology studies (376-372 and 376-376) and 2 clinical studies (376-364 and 376-369). Additional safety data in 228 subjects from one ongoing clinical study (376-374) were also reviewed for serious adverse events and withdrawals due to adverse events. This safety update summarizes safety informaton collected through the cut-off date of 02-Feb-91. If you have questions, etc. ------

SubType: NDA

CI#: 376 Sub Date: 12/27/90

Generic: Appr Date:

Product Name: Estrostep Tablets

Barcode	Ser/ Ref#	Date / To: / From:	RE/ Report Title/ Report No. / Contents/Report No./
B04605	7	Thu, May 16, 1991	Letter Re: Amendment to Estrostep NDA Item 3
		S. Sobel	Re: Reference is made to our NDA 20-130 for Estrostep (norethindrone acetate and ethinyl estradiol, USP) tablets for oral contraception submitted on Dec. 27, 1990. Enclosed within is an amendment to Item 3 of the Estrostep NDA. As described in the Dec. 27, 1990 cover letter to the NDA, and as agreed in a Oct. 26, 1990 discussion with Dr. Yuan Yuan Chiu of your division, updated stability data on full production scale lots are to be submitted to the NDA. This amendment contains the six month stability reports for the following full scale production lots: Continued - see central file copy.
		S. Brennan	
B04605	8	Wed, Jun 12, 1991	Letter Re: Response to FDA Request for Information
		S Sobel	Re: Reference is made to our new drug application (NDA 20-130) for Estrostep (norethindrone acetate and ethinyl estradiol, USP) tablets for oral contraception submitted on December 27, 1990. In response to a telephone request by Dr. Martin Bennett of your division (11-Jun-91), we are amending Item 3 of the NDA to clarify the description of the PVC blister material described on P. 159 of Item 3 (Volume 1.2). The blister package material is described as "colendered polyvinyl chloride." The word "colendered" is a typographical error which should be "calendered". Calendered polyvinyl chloride describes the process used to make the blister material. The process of forming sheets of polyvinyl chloride by pressing the material between rollers or plates is referred to as calendering. Continued - see central file copy.
		S. Brennan	
B04605		Wed, Jun 19, 1991	Letter Re: Promotion of Oral Contraceptive
		M. Taylor	Re: This letter is intended to provide information regarding the promotion of oral contraceptive drug products. It was developed jointly between the divisions of metabolism and endocrine drug products and drug marketing, advertising, and communications and should be considered informal guidance regarding acceptable promotion for these products at this time. This letter has been sent to all applicant holders for oral contraceptive products. Continued - see central file copy.
		S. Sobel	
B04605	9	Tue, Jun 25, 1991	Letter Re: Research Report Page Corrections
		S. Sobel	Re: The following research report was submitted to the original NDA on 27-Dec-90. A Single-Dose Bioavailability Study of Market-Image and Estrostep 1/35 Tablets Currently Being Used in Clinical Trials and Market-Image Tablets Prepared as a Suspension in Water: Protocol 376-372-0" Attached are corrected pages for the above report. The clinical tables 14-16 in Appendix 4 have been replaced due to minor corrections. As a result, please replace pages 341-404 of Research Report No. 764-01538. These corrections have no significant impact on study results.
		M. Taylor	

SubType: NDA

CI#: 376 | Sub Date: 12/27/90

Generic: | Appr Date:

Product Name: Estrostep Tablets

Barcode	Ser/ Ref#	Date / To: / From:	RE/ Report Title/ Report No. / Contents/Report No./
B04605		Wed, Jul 24, 1991 I. Martin S. Sobel	Letter Re: Identified Deficiencies in Application Re: Reference is made to your pending new drug application, for Estrostep-21 (norethindrone acetate and ethinyl estradiol) tablets and Estrostep-28 (norethindrone acetate and ethinyl estradiol tablets and ferrous fumarate tablets). Although we have not completed our review of your application, we have identified certain deficiencies in the application and request that you provide the following information: 1. A copy of the patient package insert (PPE) must be submitted, and the physician insert (prescribing information: PPI) must include a reproduction of the PPI. All labeling pieces must include the issue date and the maufacturer's name and address. The established name must accompany the proprietary name as required in 21 CRF 201.10(G). Continued - see central file copy.
B04606	10	Thu, Aug 22, 1991 S. Sobel M. Taylor	Letter Re: New Drug Application Re: Reference is made to your letter of 24-Jul-91 regarding our new drug application for Estrostep. Please find attached 5 copies of the physician insert (PI), patient package insert (PPI) and patient brief summary. These documents have now been typeset and include the issue date and manufacturer name and address. The established name has been added to accompany the proprietary name as required in 21 CRF 201.10(G). The PPI was submitted in draft format in the NDA in Item 4, samples, methods and labeling, Volume 1.3. We are currently in the process of revising the 21 and 28 day blister package labels to comply with the requirement in which the established name must be no less than half the height of the proprietary name. Copies will be submitted shortly. Continued - see file copy.
B04606		Fri, Sep 06, 1991	Minutes of FDA Meeting Date: 31-Jul-91 Switch of oral contraceptives to OTC status.
B04606		Fri, Sep 20, 1991 J. Hunt M. Taylor	Letter Re: Summary and Reports on Disk Re: As requested by you on 16-Sep and E. Galliers on 18-Sep, attached are the disks for the following portions of the Estrostep NDA. 1) Section 6.1. Summary of the human pharmacokinetics of norethindrone acetate and ethinyl estradiol. 2) Section 6.3. Report: (See file copy) 3) Section 6.3. Report:)See file copy) The disks are in Wordperfect 5.1 and contain primarily the text portion of the summary and reports. This information is identical to what was submitted as hard copy therefore this letter/disks have not been submitted to the NDA. The additional comparison document and reports which were presented on 16-Sep will be submitted to the division of Metabolism/Endocrine with a desk copy and Wordperfect disk copy to you.

SubType: NDA

CI#: 376 Sub Date: 12/27/90

Generic: Appr Date:

Product Name: Estrostep Tablets

Barcode	Ser/ Ref#	Date / To: / From:	RE/ Report Title/ Report No. / Contents/Report No./
B04606	11	Mon, Sep 23, 1991	Letter R: Life Table Calculations
		M. Ponnapalli	Re: Please find attached the life table calculations requested by you on 16-Sep-91. This information will be part of a submission to the division of Metabolism/Endocrine. Questions call ---
		M. Taylor	
B04606	12	Wed, Oct 02, 1991	Letter Re: Amendment No. 4
		S. Sobel	Re: Reference is made to our pending NDA 20-130 for Estrostep and our meeting of 16-Sep-91 with your division. Enclosed is the additional information on Estrostep as agreed to at our meeting. We have updated the pregnancy and adverse event charts and summaries distributed at the meeting, with new information. This document is dividied into the following 4 sections. 1) Pharmacokinetics - see file copy. 2) Product comparison - see file copy. 3) Pregnancies - see file copy. 4) Adverse events - see file copy. The formulation and process used to manufacture Estrostep for the clinical study 376-364 is the same as what we intend to use to manufacture tablets for marketing. Continued - see file copy.
		M. Taylor	
B04606	13	Fri, Oct 18, 1991	Letter Re: Additional Information Requested
		S. Sobel	Re: Please find attached additional information requested of me by Dr. R. Velagapudi, division of Biopharmaceutics, during a discussion on 16-Oct-91. Questions call ------
		M. Taylor	
B04606	14	Mon, Oct 28, 1991	Letter Re: Additional Information
		S. Sobel	Re: Please find attached the additional information requested by Dr. R. Velagapudi, division of Biopharmaceutics, by telephone on 21, 22 and 24-Oct-91. These responses were faxed to Dr. Velagapudi on 23 and 25-Oct-91. Question call ------
		M. Taylor	
B04606		Wed, Nov 06, 1991	Changes in Preclinical and Clinical
		I. Martin	In 11/89 DMEDP wrote to current manufacturers of oral contraceptives describing changes in the preclinical and clinical testing requirement for steroidal contraceptives based in part on recommendations of the world health organization and FDA's Advisory Committee for Fertility and Maternal Health Drugs.
		S. Sobel	

SubType: NDA

CI#:	376	Sub Date:	12/27/90
Generic:		Appr Date:	
Product Name:	Estrostep Tablets		

Barcode	Ser/ Ref#	Date / To: / From:	RE/ Contents/Report No./ Report Title/ Report No.
B04606	15	Thu, Nov 07, 1991	Letter Re: Estrostep Labels
		S. Sobel	Re: In response to your letter of 24-Jul-91 requesting copies of each (21 and 28 day packages) blister package configuration (label) in which the established name is no less than half the height of the proprietary name as required in 21 CFR 201.10(G), we provide the attached corrected configurations. Also requested was a potency statement on the label, if space permits. Space on the label does not permit a potency statement. Thirteen copies of the final printed labels are submitted as 7 mounted copies and 6 unmounted copies divided into 3 copies of each in 2 envelopes as requested by the division of Metabolism and Endocrine drug products. Questions call ------
		M. Taylor	
B04606		Mon, Nov 25, 1991	FDA Minutes of Our 16-Sep-91 Meeting on Estrostep
B04606	16	Tue, Nov 26, 1991	Letter Re: Update to Estrostep NDA Item 3
		S. Sobel	Re: Reference is made to our NDA (20-130) for Estrostep (norethindrone acetate and ethinyl estradiol, USP) tablets for oral contraception submitted on 27-Dec-90. Enclosed as Attachment 1 is an update to Item 3 of the Estrostep NDA. As described in the 27-Dec-90 cover letter to the NDA, and as agreed in a 26-Oct-90 discussion with Dr. Yuan Yuan Chiu of your division, updated stability data on full production scale lots are to be submitted to the NDA. Attachment 1 contains the 9 and 12 month stability reports for the full scale production lots. The 08-Feb-91 amendment contained three month data and the 16-May-91 amendment contained the six month data for these lots. Continued - see file copy.
		S. Brennan	
B04606		Mon, Dec 09, 1991	Minutes of FDA Meeting
			Date: 16-Sep-91 Minutes for internal purposes only. No minutes have been or will be submitted to the FDA as we committed to provide all the information requested at the meeting in the amendment. This amendment was submitted on 02-Oct-91.
B04606		Thu, Dec 12, 1991	Minutes of FDA Meeting
			Date: 04-Dec-91 FDA meeting to discuss proposal for a manufacturing process change for this unapproved product and the data requirements to support the change, especially with respect to bioequivalence to the product used in the clinical trials and to be marketed.

SubType: NDA

CI#: 376 Sub Date: 12/27/90

Generic: Appr Date:

Product Name: Estrostep Tablets

Barcode	Ser/ Ref#	Date / To: / From:	RE/ Contents/Report No./ Report Title/ Report No.
B04607	18	Fri, Dec 20, 1991	Letter Re: Safety Update
		S. Sobel	Re: Attached is a safety update for the Estrostep NDA 20-130. The original integrated summary of safety summarized data from one clinical pharmacology study (376-372) and one clinical study (376-364), through a cut-off date of 28-Mar-90. The 4-month safety update (ref #6) submitted 26-Apr-91 summarized the safety data from two clinical pharmacology studies (376-372 and 376-376) and three clinical studies (376-364, 376-369, 376-374). Continued - see file copy.
		M. Taylor	
B04607	17	Sat, Dec 21, 1991	Letter Re: Amendment 5
		S. Sobel	Re: Reference is made to our pending NDA 20-130 for Estrostep, our meeting of 04-Dec-91 with your division and the division of Biopharmaceutics, and a telecommunication between Mary Taylor and John Hunt of the division of Biopharmaceutics on 05-Dec-91. Attached is the following information. 1) Background information on Biopharmaceutics review of NDA; 2) Dissolution - continued see file copy. 3) Pharmacokinetics - continued see file copy. 4) Revised manufacturing process and batch records Continued - see file copy. Questions contact ------
		S. Brennan	
B04607		Mon, Jan 13, 1992	Letter Re: Additional Days for Review
		I. Martin	Re: Reference is made to your pending NDA for Estrostep-21 tablets and Estrostep-28 estradiol tablets and ferrous fumarate tablets. We also refer to the 21-Dec-91, amendment to your NDA received by FDA on 23-Dec-91. We consider your amendment a major amendment under 21 CFR 314.60 and we have determined that 120 additional days will be required for its review. The new due date is 29-May-92. Questions contact Ms. Enid Galliers.
		S.Sobel	
B04607	19	Wed, Feb 12, 1992	Letter Re: Additional Information
		S. Sobel	Re: Please find attached additional information requested by Dr. R. Velagapudi, division of Biopharmaceutics, by telephone on 10-Feb-92. These responses were faxed to Dr. Velagapudi on 12-Feb-92. Questions contact ------
		M. Taylor	

SubType: NDA

CI#: 376 Sub Date: 12/27/90

Generic: Appr Date:

Product Name: Estrostep Tablets

Barcode	Ser/ Ref#	Date / To: / From:	RE/ Report Title/ Report No. / Contents/Report No./
B04607	20	Fri, Mar 13, 1992	Letter Re: Additional Information
		S. Sobel	Re: On 02-Mar-92, Dr. R. Velagapudi from the division of Biopharmaceutics requested additional information on the dissolution method for Estrostep. Our response to this request is summarized below. A copy of this letter was transmitted to Dr. Velagapudi by telecopy on 13-Mar-92. Dissolution of Estrostep tablets is performed in 0.1 N hydrochloric acid containing 0.06% sodium lauryl sulfate. Due to the potential for hydrolysis of norethindrone acetate (NA) to norethindrone and degradation of ethinyl estradiol (EE), studies were performed to characterize the stability of both NA and EE in the dissolution medium. Continued - see file copy.
		S. Brennan	
B04608	21	Thu, Apr 16, 1992	Letter Re: Response to Request for Information
		S. Sobel	Re: Please find attached additional information requested by Ms E. Galliers for the division of Biopharmaceutics by telephone on 24-Feb and by fax on 10-Apr-92. A. Final report for Protocol 376-378. A draft report for Protocol 376-378 was submitted 2-Oct-91. The complete report is now available. Only minor editorial change have been made in the report. No sample reanalysis was done. B. Update clinical pharmacology section of labeling (continued - see letter) C. Multiple dose study protocol (Continued - see letter)
		M. Taylor	
B04610	22	Mon, Apr 20, 1992	Letter Re: Amendment 4 Revisions
		S. Sobel	Re: Reference is made to our pending NDA 20-130 for Estrostep and our submission of 2-Oct-91, Amendment 4. Upon further examination of the data for studies 376-364 and 376-369, it was discovered that two errors were made and reported in the amendment. In the 376-364 clinical study there was an error in reading and reporting of the confidence intervals for the Pearl Index for Estrostep and Loestrin. The 97.5% bound was given as the lower bound for Loestrin and the upper bound for Estrostep. Tab 1 contains the corrected page and for your reference, the original page as it was submitted 2-Oct-91. Tab 1: Pregnancies Tab 2: Serium estradiol and progestrone data clinical study 376-369 Continued - see file copy.
		M. Taylor	
B04610	23	Tue, May 05, 1992	Letter Re: Response to Request for Information
		S. Sobel	Re: Reference is made to our pending NDA 20-130 for Estrostep, our letter of 13-Mar-92 (reference No. 20) and your fax of 24-Apr-92 regarding the overall recommendation from the division of Biopharmaceutics. In our letter of 13-Mar-92, we committed to analyze dissolution samples within two hours of sampling. We will evaluate other dissolution medium to determine if the stability of the two drugs, especially norethindrone acetate, can be improved. If a medium is found in which the stability of the two compounds is enhanced, we will discuss our results with the agency. The dissolution medium and specifications will not be changed without prior approval by FDA of an NDA supplement. Questions contact ------
		M. Taylor	

SubType: NDA

CI#: 376 Sub Date: 12/27/90

Generic: Appr Date:

Product Name: Estrostep Tablets

Barcode	Ser/ Ref#	Date / To: / From:	RE/ Report Title/ Report No. / Contents/Report No./
B04610	24	Thu, Jun 11, 1992	Letter Re: Safety Update
		S. Sobel	Re: Following is a summary of the safety information for Estrostep NDA 20-130. The original integrated summary of safety summarized data from one clinical pharmacology study (376-372) and one clinical study (376-364), through a cut-off date of 28-Mar-90. The 4-month safety update (ref. no. 6) submitted 26-Apr-91 summarized the safety data from two clinical pharmacology studies, (376-372 and 376-376) and three clinical studies (376-364, 376-369, and 376-374). Continued - see file copy.
		M. Taylor	
B04610	25	Thu, Jun 18, 1992	Letter To: Update to Estrostep NDA Item 3
		S. Sobel	Re: Reference is made to our NDA (NDA 20-130) for Estrostep (norethindrone acetate and ethinyl estradiol, USP) tablets for oral contraception submitted on 27-Dec-90. Enclosed is an update to Item 3 of the Estrostep NDA. As described in the 27-Dec-90 cover letter to the NDA, and as agreed in an 26-Oct-90 discussion with Dr. Yuan Yuan Chiu of your division, updated stability data on full production scale lots are to be submitted ot the NDA. This amendment contains the 18-month stability reports for the full scale production lots and initial and 3-month results from three production scale batches using the revised drying process (Amendment 5, 21-Dec-91). Continued - see file copy.
		S. Brennan	
B04610		Thu, Jun 25, 1992	Reference to 6/19/92 meeting.
		D. Michels	Thanking agency for meeting with us. Look forward to response regarding the status of pre-approval inspections.
		W. Merino	
B04610		Thu, Jun 25, 1992	Letter sent to Agency
		Distribution	This attached letter was sent to the agency on 6/25/92, via Fed-X.
		W. Merino	
B04610		Thu, Aug 27, 1992	FDA Letter
		I. Martin	Reference is made to your NDA submitted 27-Dec-90, pursuant to Section 505 (B) (1) of the FDA act for the preparation Estrostep-21 (norethindrone acetate and ethinyl estradiol tablets and ferrous fumarate tablets). We also acknowledge receipt of your additional correspondence dated 8-Feb, 28-Mar, 19-22-26-Apr, 16-May, 12-25-Jun, 22-Aug, 2-18-28-Oct, 7-26-Nov, 20-21-Dec, 1991 and 12-Feb, 13-Mar, 16-20-Apr, 5-May, 11-18-Jun, 1992. From 19-May until 9-Jul, 1992, our investigators made an inspection of your establishment at Fajardo, Puerto Rico, with respect to the applicable methods, facilities and controls, and observed a number of important departures from FDA current good manufacturing practice regulations. You were advised at that time of these deficiencies. Continued - see file copy.
		S. Sobel	

SubType: NDA

Cl#:	376	**Sub Date:**	12/27/90
Generic:		**Appr Date:**	
Product Name:	Estrostep Tablets		

Barcode	Ser/ Ref#	Date / To: / From:	RE/ Report Title/ Report No. / Contents/Report No:/
B04610	26	Thu, Sep 03, 1992	General Correspondence
		S. Sobel	Reference is made to our NDA 20-130 for Estrostep (norethinrone acetate and ethinyl estradiol, USP) tablets for oral contraception submitted on 27-Dec-90. Additional reference is made to your letter on 27-Aug-92 that stated the application is not approvable under Section 505 (B) (1) of the act and 21 CFR 314.125(B). Reference is also made to a telephone conversation between Ms. E. Galliers and I on 25-Aug-92 regarding review of the proposed labeling and response to your then proposed 27-Aug-92 letter. In accordance with your letter and as detailed in 21 CFR 314.120 (A), we are notifying you of our intent to amend this application. Contact:
		M. Taylor	
B04610	27	Mon, Mar 08, 1993	Amendment to Estrostep NDA Item 3
		S. Sobel	Reference is made to our pending NDA for Estrostep tabs for oral contraception submitted 27-Dec-90. Enclosed is an update to Item 3 of the Estrostep NDA. We are amending the CMC section of the NDA to provide for an additional site for analytical testing of Estrostep tabs. The alternate analytical testing site for Estrostep tabs will be W-L/P-D Pharmaceutical Research Division W-L Company 170 Tabor Road MOPS, NJ 07950 Our Fajardo, PR facility will remain the sole manufacturing site. Testing will be performed at Fajardo, PR or MOPS, NJ. Fajardo will remain responsible for release of the finished product. Continued - see file copy.
		S. Brennan	
B04610		Thu, Apr 08, 1993	Information.
		I. Martin	FDA believes it is imperative to take additional steps to inform the sexually active populaton about wich contraceptives have the potential to protect against sexually transmitted diseases and which do not.
		S. Sobel	

SubType: NDA

CI#: 376 Sub Date: 12/27/90

Generic: Appr Date:

Product Name: Estrostep Tablets

Barcode	Ser/ Ref#	Date / To: / From:	RE/ Report Title/ Report No. / Contents/Report No./
B06850		Wed, Mar 02, 1994	Validity Assessment
		S. Jones	Reference is made to Dr. Carl Peck's letter to Mr. Melvin Goodes of September 30, 1992, regarding validity assessments for Parke-Davis products manufactured in our Vega Baja and Fajardo facilities. Reference is also made to our December 2, 1992 response to Ms. Stephanie Gray regarding the audit protocol and process. A report of the validity assessment audit performed by Lachman Consultant Services, Inc., for Estrostep® Tablets is enclosed. A number of cGMP compliance issues were raised in the report which we are addressing in our cGMP Action Plan submitted to Mr. Richard Davis on February 18, 1993 and our efforts in connection with Consent Decree activities. In addition, the consultants' report refers to a 5% manufacturing overage of Ethinyl Estradiol for the batches reviewed. This overage was mentioned in the original NDA submission (December 27, 1990, Volume 2, Page 018). The audit report will be reviewed with the manufacturing and QA/QC management of the Fajardo plant so that they are aware of the cGMP items raised in this report.
		W. Merino	
B06850		Mon, Mar 04, 1996	2/28/96 Final Meeting Minutes
		Distribution	Attached are final minutes from the Parke-Davis/Division of Metabolism and Endocrine Drug Products meeting held February 28, 1996. (see file copy for minutes)
		I. Martin	
B14264	0	Tue, Apr 09, 1996	Amendment to Estrostep NDA Items 3 and 4
		S. Sobel	Reference is made to our New Drug Application (NDA 20-130) for Estrostep® (norethindrone acetate and ethinyl estradiol, USP) Tablets for oral contraception, submitted on December 27, 1990, and its amendments. Reference is also made to your nonapprovable letter of August 27, 1992 (Attachment 1), and our response of September 3, 1992 (Ref. No. 26), notifying you of our intent to amend the application. According to the August 27, 1992 letter from FDA, FDA could not verify compliance with current good manufacturing practice regulations at the Fajardo, Puerto Rico facility. In addition, FDA requested labeling revisions and reiterated our commitments for Phase 4 studies. We hereby amend our application addressing the matters described in the August 27, 1992 letter. This amendment contains revised Items 3 Chemistry, Manufacturing and Controls and 4 Samples, Methods Validation, Labeling. The Notes to Reviewer in Item 3.1 summarize the revisions made to the application. Review and archival copies of each section are provided.
		W. Merino	

SubType: NDA

CI#: 376 Sub Date: 12/27/90

Generic: Appr Date:

Product Name: Estrostep Tablets

Barcode	Ser/ Ref#	Date / To: / From:	RE/ Report Title/ Report No. / Contents/Report No./
B16694	0	Fri, May 24, 1996	Amendment to Estrostep NDA
		S. Sobel	Reference is made to our New Drug Application (NDA 20-130) for Estrostep® (norethindrone acetate and ethinyl estradiol, USP) Tablets for oral contraception, submitted on December 27, 1990, and its amendments. Reference is also made to our April 9, 1996 NDA amendment. We are revising the labeling to remove the USP designation from the ferrous fumarate tablets. The blister card and carton for Estrostep Fe Clinic and Trade and the physician insert will be revised.
		L. Bloom	
B16694	0	Wed, Jul 17, 1996	Response to FDA Request for Information: CMC Amendment
		L. Rarick, M.D.	Reference is made to our New Drug Application (NDA 20-130) for Estrostep® (norethindrone acetate and ethinyl estradiol, USP) Tablets for oral contraception, submitted on December 27, 1990, and its amendments. Reference is also made to Mr. S. Koch's requests for information and new specifications during telephone conversations with Dr. L. Bloom on May 6, June 4, 11, and 18, 1996. Questions about nomenclature and the location of information in the NDA were addressed during the phone calls. This submission responds to the requests for: Introduction of specifications for impurities/degradation products of ethinyl estradiol and norethindrone acetate. A revised DMF authorization letter from VKW citing PVC Type 37.0 in accord with the packaging specifications. Justification of the use of an ethinyl estradiol excess to account for manufacturing losses. Justification of the use of an in-process test for residual alcohol levels instead of a test on the finished tablets. Four copies of the method validation package, identification of the lots to be provided to FDA for method validation, and Certificates of Analysis for the method validation lots.
		L. Bloom	
B16694		Fri, Aug 16, 1996	Method Validation Letter
		L. Bloom	The FDa will be performing method validation studies on Estrostep 21 and Estrostep Fe in connection with your NDA 20-130. In order to perform the necessary testing, please provide us with a sample consisting of the following: (see file copy for list)
		S. Senio	
	0	Mon, Sep 23, 1996	Response to FDA Labeling Questions: CMC Amendment
		L. Rarick	Reference is made to our New Drug Application (NDA 20-130) for Estrostep® (norethindrone acetate and ethinyl estradiol, USP) Tablets for oral contraception, submitted on December 27, 1990 and its amendments. Reference is also made to the September 18, 1996 fax of chemistry, manufacturing and controls labeling questions and the September 18, 1996 teleconference between Dr. Helen Davies of your Division and Ms. Mary Taylor, M.P.H. and Dr. Leslie Bloom of Parke-Davis. This submission responds to each question individually. The questions are reiterated in italics for ease of reference.
		L. Bloom	

SubType: NDA

CI#: 376 Sub Date: 12/27/90

Generic: Appr Date:

Product Name: Estrostep Tablets

Barcode	Ser/ Ref#	Date / To: / From:	RE/ Report Title/ Report No. / Contents/Report No./
	30	Wed, Oct 02, 1996	Request for Information
		L. Rarick	Reference is made to our New Drug Application (NDA 20-130) for Estrostep® (norethindrone acetate and ethinyl estradiol, USP) Tablets for oral contraception, submitted on December 27, 1990 and its amendments. Reference is also made to Ms. Kish's request in telephone conversations with Ms. Pitts on September 30, 1996 for additional copies of the proposed labeling. This submission provides for the information requested.
		M. Taylor	
	28	Wed, Oct 02, 1996	Safety Update
		L. Rarick	Reference is made to our New Drug Application (NDA 20-130) for Estrostep® (norethindrone acetate and ethinyl estradiol, USP) tablets for oral contraception, submitted on December 27, 1990, and its amendments. Reference is also made to Ms. Kish's request in a telephone conversation with Ms. Pitts on September 30, 1996 for information on a Safety Update for Estrostep. There have been no new clinical pharmacology or clinical studies, therefore we have no new safety information to provide since our last safety update dated June 11, 1992.
		M. Taylor	
	29	Wed, Oct 02, 1996	Request for Information
		L. Rarick	Reference is made to our New Drug Application (NDA 20-130) for Estrostep (norethindrone acetate and ethinyl estradiol, USP) tablets for oral contraception, submitted on December 27, 1990, and its amendments. Additional reference is also made to the request of September 30, 1996, from Ms. C. Kish of your Division to Ms. R. Pitts of Parke-Davis for the debarment certification statement for Estrostep.
		M. Taylor	